

Meperidine Withdrawal Syndrome Associated with Low Dose Short Term Use

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Abstract

Analgesics, including opioids such as meperidine are used for treatment of abdominal pain caused by acute pancreatitis. Meperidine withdrawal syndrome is usually seen after long-term use. We present here an acute pancreatitis patient who experienced meperidine withdrawal syndrome after short term use and treated successfully with tramadol and deksketoprofen.

Keywords: Meperidine; Withdrawal syndrome; Acute pancreatitis

Introduction

Acute pancreatitis is an acute inflammation of the pancreas associated with high morbidity and mortality [1]. Abdominal pain is the most common symptom of acute pancreatitis [2]. Effective management of severe pain in acute pancreatitis is important and sometimes difficult. Analgesics are the mainstay of treatment and according to the severity of the pain non-steroidal, anti-inflammatory drugs (NSAIDs), tramadol or opioids are used alone or in combination [3]. We here will describe a case of acute pancreatitis patient who used short period of meperidine infusion and afterwards experienced withdrawal syndrome.

Case Report

Sixty-years old woman was admitted to the emergency department with complaints of abdominal pain, nausea and vomiting. The physical exam was unremarkable except for marked abdominal tenderness. Significant laboratory data were as follows: White blood cells 12,900 mm³ (4,500-11,000), hemoglobin 13.1 gr/dL (13.5-18.0), aspartate aminotransferase: 113 U/L (0-41), alanine aminotransferase: 96 U/L (0-40), amylase 685 IU/L (30-110), lipase 2321 IU/L (13-60), C reactive protein: 2.2 mg/L (0-10), alkaline phosphatase: 259 U/L, total serum bilirubin: 0.9 mg/dl (0.2-1.2), gamma glutamyl transferase 203 U/L (8-61). Abdominal ultrasonography revealed millimetric gallbladder stones and concentrated biliary sludge. Intra- and extrahepatic bile ducts were dilated. Pancreas was slightly enlarged with an edematous appearance and small amount of peripancreatic fluid was present. Ranson score was 3 during admission to hospital. Patient was transferred to the intensive care unit and intravenous fluid replacement was started. In order to relieve severe abdominal pain, intramuscular diclofenac sodium 75 mg twice a day and afterwards intramuscular meperidine 50 mg subcutaneously twice a day applied to patient. However abdominal pain did not alleviate and 120 mg/day continuous IV infusion of meperidine was begun due to the algology consultation. After 24 hours of meperidine infusion and alleviation of pain, infusion doses decreased gradually and stopped at 36 hours of treatment. Within three hours after discontinuation patient

experienced complaints of palpitations, dryness of mouth, shortness of breath and sweating. She seemed as anxious, nervous and frightened. Patient was consulted by neurology, psychiatry and algology departments and consensus of these three sections was declared as meperidine withdrawal syndrome. Tramadol 4 × 50 mg/day and deksketoprofen trometamol 75 mg/day p.o. was applied to the patient. Twenty-four hours later, the patient's complaints and symptoms disappeared and treatment gradually tapered and discontinued in 36 hours.

Discussion

The diagnosis of acute pancreatitis is, in most cases, based on an acute onset of abdominal pain (upper abdominal pain, sometimes radiating to the back or the shoulders) and the absence of other acute pain-inducing abdominal conditions (e.g., peptic ulcers, bile duct diseases, or intraabdominal vascular occlusions), paired with significantly increased serum amylase or lipase (usually three times over the upper reference value) [4]. Pain is localized to the epigastrium and periumbilical regions in about two thirds of the patients, whereas in most other cases, pain is diffuse and difficult to localize.

The pain is often continuous for hours (e.g., biliary pancreatitis) or days (alcoholic pancreatitis and more severe forms of biliary pancreatitis), but can be intermittent in less than 15% of patients. The intensity is reported from "as severe as possible" to "well tolerable". In most cases, a patient with acute pancreatitis will require potent analgesics for treatment [5].

There seems to be no single cause of pain in acute pancreatitis, but several factors contribute. Pain can be due to the inflammation with direct inflammatory stimulation of pancreatic and peripancreatic nerve endings and the production of noxious and pain-inducing substances in the sensitive peritoneum. Pain is mainly due to the release of the tachykinin substance P and calcitonin-gene-related peptide [6]. The pathological activation of sensory neurons and inflammatory sequelae are known as neurogenic inflammation and appear to be important in many organ systems, including the pancreas. Factors that stimulate primary sensory neurons include hydrogen ions, heat, leukotrienes, arachidonic acid metabolites,

bradykinins, and proteases such as trypsin, all of which might participate in the generation of acute pancreatitis [7].

This pain severity might be from mild discomfort to severe ranging from tolerable. Pain control is an important step in treatment of acute pancreatitis. An observational multicenter study on the treatment of acute pancreatitis in Italy demonstrated that analgesics were graded according to the severity of the pain in routine clinical practice; patients with mild acute pancreatitis received mainly NSAIDs and tramadol, whereas patients with severe pancreatitis received a high percentage of opioids or an association of analgesics including NSAID's, tramadol, and opioids [8].

Parenteral narcotic analgesics to treat severe pain of patients with acute pancreatitis is often applied. Meperidine is an opioid with high addiction potential and depending on the use of meperidine different side effects are described and withdrawal syndrome is one of them. Meperidine effect begins rapidly, reaches the highest level at 8-12 hours, and ends in 4-5 days. Meperidine abuse and dependence have been reported especially among healthworkers and patients with chronic pain [9,10]. Literature lacks of the data related with withdrawal syndrome occurred after short-term infusion of meperidine. Our patient took two doses of 50 mg intramuscular meperidine and afterwards 36 hours of infusion in decreasing manner during the last 24 hours and signs and symptoms related with withdrawal syndrome began three hours after ceasing the infusion. Normeperidin is meperidine's metabolite and is thought to be responsible from side effects such as analgesia, sedation, irritability, hyperreflexia, tremor, myoclonus, generalized tonic clonic seizures. Our case did not experienced such side effects during treatment however after discontinuation meperidine infusion signs and symptoms emerged so we decided to describe the situation as withdrawal syndrome. Meperidine withdrawal syndrome is usually seen after the long-term use such as for chronic pancreatitis pain, malignancy-associated pain or neuropathic pain. Initially patients seem to be in discomfort, anxious and irritable without having any reason for these symptoms. Symptoms begin with a sense of unease, anxiety and alarm for which there is no apparent reason. Afterwards they progress to mild paranoid thinking and to visual and auditory hallucinations with great agitation and fear, sometimes with the patient running out of the hospital, and requiring restraint and heavy

sedation. However to the best of our knowledge we have not noticed any article mentioning about withdrawal syndrome related with short term meperidine use.

In conclusion many physicians use meperidine for different reasons either in short or long term periods. Although most of us are aware of serious side effects or addiction risk especially during long term use we should keep in mind that short term use such as for acute pancreatitis could have consequences related with side effects or withdrawal. To think the possibility of this diagnosis and tramadol and deksketoprofen trometamol treatment could rapidly and easily solve the problem.

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